BEDSIDE MEDICINE FOR BEDSIDE DOCTORS

An Open Forum for brief discussions of the workaday problems of the bedside doctor. Suggestions of subjects for discussions invited.

EARLY DIAGNOSIS OF PREGNANCY

SAMUEL HANSON, M. D. (1009 Medico-Dental Building, Stockton).—The symptoms and signs of early pregnancy are very familiar to all. The recent introduction of the Aschheim-Zondek hormone test has, however, made a radical change in the problem of diagnosis. A review of the subject and a reappraisal of the value of the classical symptoms and signs has, therefore, become necessary.

In obtaining the history and in interpreting the symptoms of pregnancy, one must first determine whether or not circumstances exist which may cause the patient to conceal or to misrepresent the facts. For example, if there is reason to believe that an abortion is sought, a negative history may largely have to be discounted. Likewise, in certain medico-legal cases, or when pseudocyesis is suspected, a positive history should be accepted with much skepticism.

Among the symptoms of early pregnancy cessation of menstruation is by far the most important one. But it is a well-known fact that amenorrhea may be due to numerous causes other than those of pregnancy. The most important among these are acute and chronic illnesses which undermine the general health; particularly tuberculosis and conditions resulting in severe secondary anemia. Endocrine disturbances also play a very important rôle, especially hypofunction of the anterior pituitary, and both hyper- and hypothyroidism. Amenorrhea of endocrine origin also occurs during lactation or during the onset of the menopause. Amenorrhea may also result from various miscellaneous causes such as changes in climate, or profound psychic disturbances such as fear or shock.

On the contrary, vaginal bleeding, which to the patient may be indistinguishable from menstruation, may occur during one or more regular monthly periods following conception. Irregular bleeding may also occur, which may be due to a threatened abortion or to an ectopic pregnancy.

However, with all due allowances for exceptional conditions, amenorrhea remains the most important symptom of early pregnancy, while regular monthly vaginal bleeding points strongly against the existence of pregnancy.

Morning nausea is perhaps next in importance to amenorrhea as a symptom of pregnancy. It occurs in about 30 to 40 per cent of all cases. It may appear as early as the second week after the first missed period. Nausea and vomiting, may of course, be due to conditions other than those of pregnancy, such as gastro-intestinal disorders, or pathology extrinsic to the gastro-intestinal tract; or it may even result from purely psychic disturbances.

Symptoms of lesser frequency and of minor importance are those due to nervous instability, such as changes in temperament, and the well-known peculiar cravings for food. Other symptoms of lesser importance are increased salivation and a sensation of fullness and tingling or burning in the breasts; also frequency of urination and constipation.

In considering the signs of pregnancy it is presumed that the findings are elicited by the hand of an experienced examiner. One who performs pelvic examinations only occasionally is seldom competent in recognizing the early signs of pregnancy, and is even less capable of distinguishing such signs from those due to pathologic conditions simulating pregnancy. A discriminating sense of touch can properly be developed only through constant practice in bimanual examinations, performed for gynecologic as well as for obstetric conditions.

Among the clinical signs of early pregnancy the one of outstanding importance is softening of the isthmus or future lower uterine segment, known as Hegar's sign. The entire uterus and cervix, of course, undergo a marked softening, but the softening of the isthmus appears earliest, and is always more pronounced than that of the fundus and cervix. Under favorable circumstances this sign can be elicited by bimanual examination as early as the second or third week after the first missed period; and in the great majority of cases it becomes unmistakable within one or two weeks following the second missed period. However, under certain conditions, as in cases of obesity, or when the coöperation of the patient is unsatisfactory, it may be difficult to recognize this sign until a later period.

Softening of the cervix becomes noticeable one or two weeks after Hegar's sign is first recognizable. The cervix of the nonpregnant state is almost of cartilagenous consistency. During pregnancy it undergoes a marked softening, approaching the consistency of the surrounding soft tissues (Goodell's sign). At the same time there is a rapid growth in the body of the uterus, so that within one or two weeks after the second missed period it attains approximately twice its ordinary size. Closely associated with the growth in size there is a uniform softening of the uterus; the organ becoming of cystic consistency and of spherical contour by the time the third menstrual period is missed.

At the end of the third month of pregnancy a generalized bluish discoloration of the vaginal

mucosa and cervix becomes noticeable in most cases. This is generally referred to as Jacquemin's or Chadwick's sign. At this stage of pregnancy, intermittent painless contractions of the uterus also begin to appear (Braxton-Hicks sign).

The above description of the symptoms and signs of early pregnancy applies only to the normal, uncomplicated condition of the pelvic organs. There is an endless variety of possible coexisting pathologic conditions which may modify or mask one or more of the important signs. Conversely, there are many pathologic conditions which may present signs indistinguishable from those of pregnancy. Space does not permit a discussion of more than a few of the more important of these complicating conditions.

Hegar's sign may be modified by a distortion or an induration of the lower uterine segment due to the presence of a fibroid in the isthmus. A coexisting pregnancy may, therefore, be overlooked. On the other hand, the presence of a fibroid or other neoplasm in the fundus, associated with a sharp retroflexion, may result in a marked passive congestion, and considerable softening of the isthmus, which may lead to a wrong diagnosis of pregnancy.

Goodell's sign, softening and enlargement of the fundus, and cyanosis of the mucosa, are even more apt to be simulated by conditions other than those of pregnancy. Fibroids and other uterine neoplasms, or even pelvic conditions of inflammatory origin which cause pelvic congestion, may produce all of these signs. With fibroids or other new growths there is, however, usually an induration rather than a softening, and even in cases of cystic degeneration the softening is limited to definitely circumscribed areas and lacks the uniformity characteristic of pregnancy.

Softening and enlargement of the uterus, which sometimes occur in pelvic inflammatory disease, are usually associated with pain, tenderness, adnexal thickening, and fixation of organs. The same is true of tubal pregnancy.

Subinvolution, which often persists for months after an abortion or a puerperal infection, may mimic very closely the softening and enlargement of the normal pregnant uterus. The same may be said of the findings in a hematometra or in a pyometra. On the other hand, a pregnancy in an incarcerated retroflexed uterus may be confused with a pelvic hematocele or a chronic pelvic abscess.

Pathologic conditions of the adnexa, particularly a cystic ovary or a hydrosalpinx located in the anterior or in the posterior cul-de-sac may easily be mistaken for a pregnant uterus, unless a careful search is made for the relatively small displaced hard uterus. Even a full bladder in an obese or poorly coöperative patient may be confused with a two or three months' pregnancy.

The remaining signs of early pregnancy are less constant and less characteristic. Among these may be mentioned the breast signs, which consist of a uniform enlargement of both breasts, a hypertrophy of the tubercles of Montgomery, an increased pigmentation of the primary and secondary areolae, and a secretion of collostrum. Another of the signs of minor importance is pigmentation of the face, the so-called "mask of pregnancy."

Of the many laboratory tests proposed, the Aschheim-Zondek hormone test is the only one which has gained universal recognition as a dependable sign of pregnancy. Its value is particularly great when a diagnosis must be made early in pregnancy—during the second or third week after the first missed period, since at this early stage Hegar's sign is still negative or doubtful in most cases. The hormone test may also prove to be of material assistance later in pregnancy, in the differential diagnosis of surgical conditions of the abdomen, particularly under circumstances where the history is atypical or unreliable, or when the important signs are not definitely positive. Under ordinary circumstances, however, it should seldom be necessary to resort to the hormone test after the second month, since at this stage of pregnancy the symptoms are usually unmistakable and the signs are strongly positive.

Needless to state, a diagnosis of pregnancy should never be made on the basis of the laboratory report exclusively. The physician should rather make a serious attempt to arrive at a diagnosis on the basis of clinical evidence alone, since the laboratory test involves loss of time, is an added expense to the patient, and, most important of all, it is not infallible. Furthermore, the clinician must study symptoms and signs for the sake of his own mental discipline, since too quick an acceptance of a ready-made diagnosis handed down from the laboratory inevitably tends to impair his diagnostic acumen.

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EDWARD N. EWER, M. D. (251 Moss Avenue, Oakland). — A fertilized ovum lodged in the uterine tube may rupture when but ten or fifteen days old. The next menstruation may be a few days overdue, or there may be no period of amenorrhea before the rupture. Such a condition would be impossible of diagnosis in advance of the accident. So, in some cases, it is evident that "early diagnosis" resolves itself into the interpretation of a sudden abdominal crisis of major proportions.

Fortunately, the behavior of the misplaced ovum, in the majority of cases, is such that its presence can be determined before the danger stage is reached. Attention may be attracted by some of the usual symptoms of early pregnancy, but they do not correlate true to form. One month amenorrhea is noted in about 60 per cent; nausea, pain or tingling in the breasts with colostrum in about 15 per cent; softening of cervix, but not Hegar's sign, occasionally; and cyanosis of the vaginal mucosa occasionally. If pronounced, most of these signs indicate intra- rather than extra-uterine pregnancy. Increased anteflexion of the uterus, with slight enlargement not commensurate with the stage of pregnancy, is often found.

Lorrincz suggested in 1928 that a *uterine* gestational enlargement could be differentiated, if easily palpable, by the intravenous injection of small amounts of posterior pituitary extract, and noting bimanually the immediate contraction of the organ.

The studies of many case series show that about one-third of the patients had had pelvic operations, and the same number gave a history of pelvic infections, usually of mild degree.

The first symptoms of direct diagnostic importance occur when some disturbance begins in or about the aberrant gestation sac. The beginning of tubal abortion, or slight rupture with seepage of blood into the peritoneal cavity, causes pain and usually the beginning of the well-known menstrual irregularities. These two symptoms—pain and uterine bleeding—are often coincident. They are both subject to remissions. The pain is severe, moderate or slight, and is described as colicky in over one-half, lancinating in one-third, and aching in the rest of the cases.

The bleeding, as a rule, is less profuse than in the abortion of an intra-uterine pregnancy, and the blood is not so bright. It is usually of a brownish viscid character. Shreds of decidua may be found in the discharge, but whole uterine casts generally only follow sudden complete rupture or operation upon the tube. Casts or large portions of decidua are not often discovered.

If a curettage is done under the belief that uterine abortion is taking place, decidua may or may not be found. Many investigators state that its formation in the uterus is not constant. If decidua without villi is secured by curettage or in the discharge, it is of diagnostic importance. Of course, if villi are found, it is assumed that an ovum must have been implanted in the uterus.

If the bleeding has been sufficient to warrant the belief that an intra-uterine ovum if present is disrupted, many countenance diagnostic curettage. Especially may this be agreed to if at the same time a suspicious noninflammatory mass in the pelvis can be palpated, and preparations are made to follow with abdominal section if ovum tissue is not found.

A mass not palpable before interruption may often be sufficiently swollen by bleeding in and around it to be palpable thereafter. The mass is likely to be boggy, movable, and not markedly tender.

Many curettements in the presence of extra-uterine pregnancies have been done in the belief that the bleeding was due to incomplete uterine abortions; and through negligence in not securing proper laboratory identification of the tissue, tubal pregnancy has been allowed to progress till frank rupture had occurred. All tissue removed should be examined for villi, if the supposed ovum is not grossly and with certainty identifiable.

After such curettage has been done the pain continues or reappears, bleeding will soon recur, and careful palpation will then disclose the tubal mass which was not discernible at the time of the curettage. The writer has seen two such cases in which it was thought the palpable mass was tubal inflammatory reaction caused by the curettage. Blood sedimentation tests eliminated that fear in each instance.

In view of the frequency of tubal inflammation in the history of these patients, it is not perhaps surprising to note in hospital statistics the frequency of the admission diagnosis of acute salpingitis. The next most frequent mistake in diagnosis seems to be incomplete abortion. Twisted pedicle ovarian cysts are sometimes confusing and, like tubal pregnancies, they present slow sedimentation rates. They may also be attended by vomiting, rapid pulse, and shock. Time is a factor in evaluating sedimentation rates and neglected cysts becoming infected, and old degenerating hematoceles may be attended with rapid rates, as in salpingitis.

The leukocyte count is generally considered of no importance. It may be as low as 5,000 or as high as 40,000. Fever is not common in early cases.

Along with or after the appearance of the conditions described come the symptoms associated with internal hemorrhage. They depend in severity upon the amount and suddenness of the hemorrhage. They are pain, moderate to severe, often sudden in onset, *faintness,* shock or collapse, thready rapid pulse, pallor, and air hunger. Faintness is an important symptom and is present in some degree in every case. Shoulder or chest pain (Lafont sign), a reflex from subdiaphragmatic peritoneal irritation by the blood, is said to be present in 10 per cent of the cases, and indicates free bleeding. The amidopyrin test for internal hemorrhage is described as positive in over 90 per cent of the cases. Aspiration of the pouch of Douglas through the vaginal vault is comparatively safe, but many prefer a more thorough and certain exploration through a colpotomy opening. In the latter case, where blood is found, it is advisable to stitch the opening to prevent infection, and treat through an abdominal section.

In tubal abortion, or even tubal rupture, the amount of blood may be small; but its presence invariably causes faintness and pain.

A typical case of tubal abortion, in contrast to the fulminant or so-called "tragic" condition mentioned at the beginning of this discussion, occurred as follows: A woman of twenty-five, who had missed a period by a few days, felt suddenly faint upon attempting to get out of bed. She walked across the room, complained of pain in the lower abdomen, lay down upon a couch and remained there several hours. The faintness soon disappeared; but the pain, while less severe, continued. Her physician was finally called, tubal pregnancy was diagnosed and, upon operation, a small ovum was found protruding from the tubal ampulla, and an ounce or two of small clots were present in the pelvis. Early diagnosis and treatment possibly forestalled further and more dangerous bleeding.

Summary.

1. The first symptoms are due to some disturbance of the growing ovum in the tube. They are faintness, pain, and irregular, usually scanty, uterine bleeding.

2. The history often discloses previous pelvic inflammatory disease or lower abdomen operative procedures.

3. There is a history of at least one missed menstruation in over half the cases. Other early symptoms of pregnancy are quite unreliable.

4. Tubal pregnancies are often confused with tubal inflammations and uterine abortions. Sedimentation tests will identify the former, and tissue examinations the latter.

5. Pulse, blood pressure and temperature changes are not early phenomena.

6. When internal hemorrhage is suspected, the amidopyrin urine test and aspiration of the cul-de-sac may be valuable.

7. Most palpable noninflammatory masses in the pelvis call for laparotomy. Especially is this true both for diagnostic and treatment purposes when such masses are associated with signs of ectopic pregnancy.

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ADOLPH W. KOSKY, M. D. (704 Bay Cities Building, Santa Monica).—With the perfection of the Aschheim-Zondek pregnancy test and its modifications, determination of the gravid state has become very much simplified.

However, there are still some points of differential diagnosis which one must take into account. Furthermore, in this question, as in others, we must not lose sight of the clinical side of medicine, even though our laboratory aids have become of great importance and value.

Probably the most common source of confusion in the early diagnosis of pregnancy results from the presence of uterine myomata of the interstitial or submucous variety. Usually the regular recurrence of menstruation or the presence of menorrhagia helps to decide the diagnosis of a neoplasm. The uterine tumor is harder and firmer in consistency; its growth is slower and Hegar's sign is absent.

If pregnancy exists concomitantly with a myoma, then frequently a positive diagnosis can only be made through one of the laboratory tests.

Extra-uterine pregnancy may be difficult to differentiate from intra-uterine pregnancy, with threatened abortion. The laboratory tests give the same results in both instances: positive if fetal life still persists, and negative if death has supervened within eight or ten days previous to the time of making the test.

Where history and physical examination do not make the diagnosis clear, I believe that one is justified in exploring the uterine cavity first. Its contents should indicate the presence or absence of gestation elements, and thus make the diagnosis sure.

An ovarian cystoma may prove puzzling, although on careful examination the uterine fundus may be found displaced in some direction and the tumor is found in one of the lower lateral quadrants; it also is more fluctuating than is the gravid uterus.

A large ovarian cyst may also be confused with a polyhydramnios, but the absence of fetal movements and heart tones should make the diagnosis clear.

Malignant diseases commencing in the cervix may be mistaken for pregnancy, although the early changes which take place in the cervix, the development of a foul, bloody discharge, and the characteristic systemic symptoms of malignancy should establish the diagnosis. A uterine sarcoma is also most difficult to differentiate, because of the symmetrical enlargement of the uterus and the amenorrhea which it produces.

A prolapsed kidney or spleen may simulate a pregnancy until the prolapsed organ is replaced and the outline of the uterus is palpated bimanually.

Sometimes difficulty arises in differentiating between ascites and pregnancy with excessive amniotic fluid. Also tuberculous peritonitis, with encysted fluid, may give findings similar to amniotic fluid. Here again, careful history of the case and failure to recognize fetal heart sounds and movements help establish the diagnosis.

During the early months, pregnancy must also be distinguished from hematometra, pelvic inflammatory swellings of the ovaries and broad ligaments, as well as exudates of an inflammatory nature; also from pyometra, cystic and solid tumors of the adnexal regions and chronic metritis.

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GERTRUDE MOORE, M.D. (2404 Broadway, Oakland).—For centuries scientists have searched for a satisfactory, practical laboratory method for the early diagnosis of pregnancy, with naught but failure until the development of the hormone test now in common use. This test is based upon the facts that the anterior pituitary increases in size and functional capacity during pregnancy, and that the abundance of hormone so produced is excreted in sufficient concentration in the urine to produce, in properly selected animals a maturing of the Graafian follicle, ovulation, and luteinization.

In order that any test for pregnancy be acceptable in practice, it must be universally present in this condition, and must not exist in other common conditions; or if it does so exist, these conditions must be easily differentiated from pregnancy, or be so rare as to be inconsequential. A review of the literature shows that the test lives up to this high standard, for in the hands of numerous workers, over a period of years, it has given an accuracy of from 95 to 99 per cent. This is a splendid showing indeed, and attests the fact that it is built on a sound scientific premise; but it is a biologic test, and by the very nature of things cannot be 100 per cent perfect.

Its usefulness in the hands of the practicing physician depends upon a clear understanding of its fallacies, and a knowledge of the conditions under which false negatives or false positives may be obtained. False negatives may be divided etiologically into two main groups: (1) biologic faults in the patients, and (2) errors in technique. Biologic faults in the patient fall, naturally, into two classes—those conditions in which the hormone is not produced in sufficient quantity to give a positive test, and those in which a hormone produced in adequate quantity is not excreted in concentrated form.

It is well known that anterior pituitary hyperactivity begins very early in pregnancy, as soon as the ovum is implanted, but the time required to reach a high concentration varies in different individuals and, in our experience, does not reach a satisfactory high level before the end of the fourth week of pregnancy. We realize that the literature tells us that the test should be positive at the first missed menstrual period, but in this our experiences differ from those of other workers.

It is quite evident that an inactive or pathologic pituitary may be so inadequate as to give a false negative test. Such an endocrine disturbance may be limited to the pituitary, or it may involve the entire endocrine chain. If this occurs, thyroid dysfunction commonly predominates the picture, and pathology of the anterior pituitary is made out only upon careful study. Frequently patients are encountered with clinical evidences of endocrine pathology, either purely pituitary or polyglandular in type, who, though pregnant, fail to give positive tests until the pregnancy is far advanced.

Lack of concentration of the hormone in the urine is, in the main, due to kidney dysfunction. It is common practice to use as the test specimen the first urine of the morning—that is, the concentrated night urine—for the reason that the hormone must be present in a fairly high degree of concentration. Patients who are suffering from kidney disturbances, and are therefore unable to concentrate their urine, will present us with specimens wholly inadequate. Likewise, it must be remembered in this connection that certain individuals have a high kidney threshold for the hormone, and it is not excreted in a form sufficiently concentrated to induce the ovarian changes in the rabbits until late in the pregnancy.

The only errors in technique of interest to the clinician are those related to the details of obtaining and handling the specimens. It is a well-known fact that urines which contain sufficient hormone to give positive findings will become inactive in this particular if allowed to stand at a moderately high temperature for a few hours, and a false negative finding may result. It is necessary, therefore, that the urine reach the laboratory as soon after voiding as possible, or if this is impossible, that it be chilled promptly and so kept until it is delivered to the laboratory. It is quite important to be sure that the urine is the urine of the patient in question, especially if there is any medico-legal problem under consideration.

While false negatives are distressing enough, false positives are of much graver significance and would render the test valueless if they occurred; but they do not worry the laboratory worker for the reason that there is only one group of conditions which may cause confusion, and this group, as will be seen later, may be differentiated from normal pregnancy. There are, however, a few conditions which must be mentioned for completeness, and which may confuse us if we are not aware of them.

First, patients transfused with the blood of pregnant women will give a positive reaction in from two to twenty hours. While this is an interesting phenomenon, it is of no practical importance for the reason that pregnant women are not commonly used as donors, and women who have recently received transfusions are not commonly immediately subjected to tests for pregnancy. Second, patients receiving anterior pituitary hormone injections will give positive findings, but this, of course, is not important for the reason that the physician administering the hormone will not undertake a test to determine its presence. Third, it is said that occasionally false positives occur at the menopause, due to the vigorous attempt on the part of the pituitary to stimulate a dying ovary. While the pituitary is particularly active under these conditions, it does not produce hormone in sufficient quantity or type to give reactions which are confusing in the hands of competent workers. Fourth, we come to the only group of conditions which gives true false positive reactions. They are hydatidiform mole and chorio-epithelioma. But these two conditions give some clinical evidence of their presence and, when suspected, they may be differentiated from normal pregnancies by the dilution test. For it is a well-known fact that the hormone exists in these conditions in a concentration of from ten to fifty times that found in normal pregnancy.

Summary.

1. Do not attempt the test until pregnancy is from four to six weeks old, unless there is some such urgent need as a suspected ectopic gestation.

2. If the test is negative and conditions warrant, repeat in one or two weeks. A somewhat longer period would be allowed in cases of endocrine dysfunction.

3. Be sure that the urine is the concentrated night specimen, submitted fresh, and that it is the urine of the patient.

4. Be sure that the patient is receiving no anterior pituitary hormone injections.

5. If there is any evidence of chorio-epithelioma or hydatidiform mole, titer the urine.

6. Be sure that the test animals are sufficiently mature to permit of stimulation, that they have been kept in isolation for a period of thirty days, and that more than one animal is used for each test.